

REMARKS

Claims 23-27, 30, 31, 35, 37-40, and 43-49 are pending. The pending claims stand rejected under 35 U.S.C. §103(a). Applicants respectfully traverse these rejections for the reasons set forth below.

Rejections under 35 U.S.C. §103

Claims 23-27, 30, 31, 35, 37-40, and 43-49 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Verbruggen et al. (*J. Rheumatol.* 26: 1663-1671, 1999; herein “Verbruggen”) and Hauselmann et al. (*Am. J. Physiol.* 271: C742-C752, 1996; herein “Hauselmann”) in view of Rosenberg et al. (U.S. Patent Application Publication No. 2003/0161884; herein “Rosenberg”) and further in view of Kavalkovich et al. (*In Vitro Cell. Dev. Biol. – Animal* 38: 457-466, 2002; herein “Kavalkovich”), Ronghua et al. (*Carbohydr. Polym.* 52: 19-24, 2003; herein “Ronghua”), Kawada et al. (*Arch. Dermatol. Res.* 291: 542-547, 1999; herein “Kawada”), and Rihova (*Adv. Drug Deliver. Rev.* 21: 157-176, 1996; herein “Rihova”).

As asserted by the Examiner, Verbruggen (a reference published by Applicants) teaches “an *in vitro* method for the cultivation of chondrocytes, comprising the step of contacting chondrocytes (chondrogenic cells) with 10 µg/ml polysulphated polysaccharides, chondroitin polysulfate and xylosan polysulfate” (Office Action, page 4). The Examiner then combines the teachings of Verbruggen with Hauselmann and Rosenberg, stating that Hauselmann teaches proteolytic degradation of aggrecan molecules in articular cartilage matrix and Rosenberg teaches the “heparin-like effect” of polysulphated alginate. The Examiner comes to the conclusion that the skilled person would recognize the interchangeability of polysulphated alginate and chondroitin polysulphate since they are both polysulphated polysaccharides with a heparin-like effect (e.g., inhibiting the coagulation of blood and the development of thromboses). Applicants

respectfully disagree and submit that polysulphated polysaccharides are not interchangeable.

Turning first to the teachings of Verbruggen, Applicants note that the Examiner's citation from the Abstract of Verbruggen is incomplete, as the Abstract refers to heparin, chondroitin polysulphate, and xylosan polysulphate, not just chondroitin polysulphate and xylosan polysulphate. Verbruggen concludes that heparin-like molecules (i.e., heparin, chondroitin polysulfate, and xylosan sulfate) have different and unpredictable effects on chondrocyte development. In support of this conclusion, Verbruggen states that "[x]ylosan sulphate and chondroitin polysulphate, but not heparin, significantly increased total ³⁵S incorporation rates" (Abstract; emphasis added). This teaching is reiterated on page 1670, second paragraph, wherein Verbruggen states:

In conclusion, it can be stated that the polysulphated polysaccharides xylosan polysulphate and chondroitin sulphate, but not heparin, improved aggrecan synthesis by differentiated human articular cartilage cells in culture. (Emphasis added)

Thus, different heparin-like molecules affect chondrocyte development in dissimilar and unpredictable ways, and heparin-like molecules may not be indiscriminately interchanged during chondrocyte cultivation, as suggested by the Examiner and resulting in the Examiner's combination of Verbruggen and Rosenberg. Rosenberg teaches pharmaceutical compositions that include heparinoids, such as sodium alginate sulphate. Rosenberg describes heparinoids as "a group of substances with a heparin-like effect, i.e., heparinoids inhibit the coagulation of blood and the development of thromboses" (§[0021]). One of skill in the art, however, would not be motivated to combine Rosenberg with Verbruggen since Verbruggen teaches away from using heparin-like molecules interchangeably in chondrocyte cultivation. Furthermore, Rosenberg is completely silent on the use of heparinoids in the context of cartilage or chondrocytes.

Hauselmann, Kavalkovich, Ronghua, Kawada, and Rihova fail to remedy the deficiencies of the Verbruggen and Rosenberg references by failing to provide the

motivation to use polysulphated alginate for chondrocyte cultivation. For the reasons provided above, Applicants respectfully submit that the claims are patentable over the cited references, and the §103 rejection should be withdrawn.

CONCLUSION

In view of the foregoing remarks, Applicants submit that the application is now in condition for allowance and such action is respectfully requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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